REMARKS/ARGUMENTS

Claims 1, 3, 8 and 11-17 are active in this case.

Support for the amendment to Claim 1 is found in previously pending Claim 2.

Support for Claim 11 is found page 7, lines 5-6.

Support for Claims 12-17 is found in amended Claim 1 and the specification on pages 6-7.

All pending claims are directed to the elected subject matter.

The specification is amended to provide a new Abstract, provide the section headings requested by the Office, and include a proper notation to the trademark product referred to on page 13.

No new matter is added by these amendments.

The rejection of Claims 1-3 and 8 under 35 USC 112, first paragraph is respectively traversed because the specification provides suitable guidance to make and/or use the claimed invention without undue experimentation. In particular, the specification on pages 6-7 describes, "[t]he inventors have now found, unexpectedly, the presence, in inflammatory skin lesions, both of 20 macrophages expressing the HLA-G protein, which are located in the dermal papillae, and of infiltrating CD3 T lymphocytes expressing a receptor for inhibiting cytotoxic functions which is recognized by HLA-G, such as for example the ILT2 receptor.

The inventors have shown that the dominant membrane- bound isoform HLA-G1 and the soluble isoform HLA-G5 are expressed only in inflammatory skin lesions, whereas no HLA-G protein is detected in healthy skin. ***[see figures 1 and 2]***

The inventors have also shown that the HLA-G protein, and in particular an isoform comprising at least the α1 domain of HLA-G, is capable of inhibiting the proliferative functions and the cytotoxic functions of T lymphocytes. ***[see figures 4 and 5].***"

Taken together then, the specification provides ample evidence of a nexus between HLA-G expression and the inhibition of T-lymphocytes, a common thread involved in various inflammatory skin conditions, psoriasis being only one example (see Claim 11). Therefore, it is requested that the enablement rejection be reconsidered in light of the evidence provided in the specification.

Moreover, in support of the rejection, a publication by Aractingi et al is cited (see page 5 quoting page 76 which states "Future analysis, such as function studies in animal models, will be needed to ultimately assess the role of HLA-G in psoriasis." However, the Office's reliance on this paper, generally, and this quote, specifically, is misplaced. The quote does not provide any indication that the HLA-G would not have the effect on inflammatory skin conditions, such as psoriasis, but rather that it will be necessary to dig deeper to understand the molecular basis for the mechanism of action. It should be appreciated that many therapies exist, which work quite well, without understanding the complete underlying molecular basis for those therapies.

In view of the above, reconsideration and withdrawal of this rejection is requested.

The rejections of Claims 1 and 2 under 35 U.S.C. §§§ 102(a), (b) and (e) in view of U.S. patent no. 5,753,625 ("US '625) and the paragraph bridging pages 4 and 5 of the specification is not tenable because US '625 does not describe the treatment of inflammatory conditions, including psoriasis, with the **whole** $\alpha$1 domain of soluble HLA-G or the **whole** soluble HLA-G. Rather US '625 effectively describes treating insulin dependent diabetes mellitus (IDDM) with **fragments** of the MHC class I antigen $\alpha$1 domain.

As discussed in US '625, the "invention" is useful for inhibiting autoimmune diseases, generally, using a specific fragment (positions 70-91) of the MHC Class I antigen (see col. 2, lines 40-46). In accordance with this description, US '625 further describes

specific peptides or oligopeptides of this type (see col. 3 and Table 1 in col. 8). Notably, in the formula provided in col. 3, the amino acid positioned at 76 must always be a valine (see col. 3, line 40) whereas In the $\alpha$1 domain of the HLA-G exemplified in the specification, a methionie is present (see SEQ ID NO:1 and the specification on page 8, line 24.

In col. 5, various diseases are listed, including psoriasis and IDDM, with IDDM the only disease specifically exemplified in the examples.

Thus, what becomes clear is that US '625 does not provide any description for the treatment of inflammatory skin conditions (such as psoriasis—see Claim 11) using the whole soluble forms HLA-G or whole $\alpha$1 domain of HLA-G as claimed.

The reliance on the specification on pages 4-5 in support of this rejection is misplaced. Simply acknowledging that psoriasis is an inflammatory pathology does not provide the necessary disclosure to devise and select the treatment. Moreover, as discussed, US '625 simply discusses autoimmune diseases generally (with IDDM as exemplary) and does not lead one to the claimed method.

Accordingly, reconsideration and withdrawal of these rejections is requested.

The rejection of Claims 1-3 and 8 under 35 U.S.C. § 103(a) in view of US '625, U.S. 5,417,986 (US '986), and the specification at pages 4-5 is not tenable because the teachings of US '986 do not compensate for the deficiencies of US '625 and as such the combination does not describe or suggest all of the limitations of the claims.

As discussed above pertaining to the rejection under § 102, there are fundamental differences between US '625 and the claims (with the cited paragraph from the specification not providing any further basis to suggest the claimed method). The '986 patent is cited merely to fill-in the void of specific dosage quantities recited in Claims 3 and 8 (see Office Action at page 7, paragraphs 6 and 7). The usefulness of US '986 in filling in this void is

misplaced because the teachings of US '986 relates to vaccines and not generally applicable to the treatment of autoimmune conditions as in US '625. Therefore, contrary to the assertion outlined in the Action, one would not have been motivated to combine these quite different descriptions. Nonetheless, the combination of disclosures fails to describe or suggest the treatment of inflammatory conditions, including psoriasis, with the **whole** $\alpha$1 domain of soluble HLA-G or the **whole** soluble HLA-G for the simple fact that US '625 effectively describes treating insulin dependent diabetes mellitus (IDDM) with **fragments** of the MHC class I antigen $\alpha$1 domain.

Reconsideration and withdrawal of this rejection is requested.

The rejections of Claims 1 and 2; and 3 and 8 under 35 U.S.C. § 103(a) in view of U.S. 625, WO98/37098, and the specification at pages 4-5 is untenable.

First, as requested, an English translation of the WO98/37098 is attached.

As discussed above pertaining to the rejection under § 102, there are fundamental differences between US '625 and the claims (with the cited paragraph from the specification not providing any further basis to suggest the claimed method). The WO application is cited merely to fill-in the void of certain HLA-G isoforms (see page 8 of the Action). However, the disclosure of this WO application relates to the expression of HLA-G genes on the cell surface (see page 5, 1st paragraph) and there use for inhibiting the activity of killer cells such as NK cells (see page 6).

What is missing from the combination of cited art (even in view of the paragraph bridging pages 4-5 of the specification) is some guidance to select the **whole** $\alpha$1 domain of soluble HLA-G or the **whole** soluble HLA-G for the treatment of inflammatory skin conditions, such as psoriasis. In fact, one would not have simply substituted any of the HLA-G forms discussed in the WO application for the peptides and oligopeptides specifically

described in the US '625 disclosure because doing so would go directly against the teachings of US '625, something that is not permitted under U.S. patent law.

Reconsideration and withdrawal of both rejections is requested.

The rejections of Claims 1-2; and 3 and 8 under 35 U.S.C. §103(a) in view of U.S. '625, WO '098, US 2003/0162175 (US '175) and the specification at pages 4-5 is traversed.

US '175 was filed as a continuation-in-part application of a PCT application filed on December 21, 2000 with an apparent earlier provisional filing date of December 22, 1999. The present application was filed as a 371 of a PCT filed on June 16, 2000 with priority to a French application filed on June 18, 1999 (before the earliest apparent filing date of US '175). To perfect priority to Applicants' French application, a certified copy and a certified English translation of the same is enclosed.

Reconsideration and withdrawal of these rejections is requested.

The IDS submission of June 1, 2004 was not a citation of prior art, but to bring to the Office's attention a potentially related application for the Examiner's consideration. That application is 10/788,374 published as US 2004/0209296 and is listed on the PTO Form 1449 filed herewith.

A Notice of Allowance for all pending claims is requested.

Respectfully submitted,

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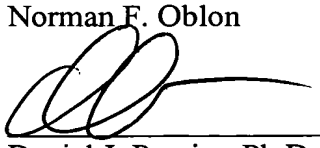

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